08/035,427

PATENT Docket 488P1C2

c'el.

application of U.S. Ser. No. 07/196,909 filed May 20, 1988, now abandoned.--

On page 20, line 19, change "210" to --218--.

IN THE CLAIMS:

Please cancel claims 18-23, 29, 61 and 66, without prejudice.

Please amend the remaining claims as follows:

- 1. (Amended) A fibrinolytically active human tissue plasminogen activator (t-PA) amino acid sequence variant [that exhibits fibrinolytic activity and contains one or more glycosylation sites at regions that are not glycosylated in the corresponding native plasminogen activator] having one or more amino acid substitutions which provide an Asn-X-Ser or Asn-X-Thr tripeptidyl sequence that starts at an amino acid position selected from the group consisting of amino acid positions 57 to 61, 63 to 69, 99, 101, 103 to 105, 106, 107, 109, 112 and 250 of the amino acid sequence of native human t-PA, wherein X is any amino acid except proline, and having N-linked glycosylation attached to the Asn within such tripeptidyl sequence.
- 11. (Twice amended) The variant of claim 1 that [contains] is selected from the group consisting of variants having (1) [a serine at position 39 of the native t-PA, (2)] an asparagine at position 50 of the native t-PA, [(3)] (2) a serine at position 60 of the native t-PA, [(4) an asparagine at position 64 and a serine or threonine at position 66 of the native t-PA, (5) an asparagine at position 65 and a serine or threonine at position 67 of native t-PA, (6)] (3) an asparagine at position 67 of native t-PA, [(7) an asparagine at position 78 and a serine or threonine at position 80 PA1077gd/am

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of the native t-PA, (8) an asparagine at position 79 and a serine or threonine at position 81 of the native t-PA, (9) an asparagine at position 80 and a serine or threonine at position 82 of the native t-PA,] (4) an asparagine at position 99 and a serine or threonine at position 101 of the native t-PA, (5) an asparagine at position 101 of the native t-PA, [or (10)] (6) an asparagine at position 103 of the native PA, (7) an asparagine at position 104 of the native t-PA, (8) an asyaragine at position 105 and a serine or threonine at position 107 of the native t-PA, (9) an asparagine at position 106 and a serine or threonine at position 108 of the native t-PA, (10) an asparagine at position 107 of the native t-PA, (11) an asparagine at position 109 and a serine or threonine at position 111 of the native t-PA, (12) an asparagine at position 112 of the native t-PA, or (13) an asparagine at position 250 of the native t-PA [or (11) a combination of any two or more of (1) to (10) above].

(Amended) The variant of claim 11 wherein the variant [contains] is selected from the group consisting of variants having an asparagine at either amino acid position 67 or [at position] 103, or [at both positions] having an asparagine at amino acid position 105 and either a serine or threonine at amino acid position 107 of the native t-PA.

^{(130.} The variant of claim [29] 1 wherein the [substitution is at] variant has an additional alteration selected from the group of alterations consisting of alanine substituted at amino acid position(s) 267, 283+287, 296-299, 303-304, 331-332, 339+342, 347-349+351, 364-366, 408, 410, 416-418, 426-427+429-430, 432+434, 440, 445+449, 449+453, 460+462, or 477 of the [corresponding wild-type] amino acid sequence of native human t-PA, where "+" indicates [alterations] the substitution of alanine only at the positions designated, and the "-" indicates [alterations] the substitution of PA1077gd/am